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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/808,129	03/24/2004	Keith R. Hildebrand	P-20904.00US	4529

27581 7590 11/30/2005

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EXAMINER	
STITZEL, DAVID PAUL	
ART UNIT	**PAPER NUMBER**
1616	

DATE MAILED: 11/30/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/808,129	HILDEBRAND ET AL.	
	Examiner	Art Unit	
	David P. Stitzel, Esq.	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-45 and 51* is/are pending in the application.

4a) Of the above claim(s) *46-50* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-45 and 51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

OFFICIAL ACTION

Restriction/Election

Restriction to one of the following inventions is required under 35 U.S.C. § 121:

I. Claims 1-45 and 51 are drawn to a sterile injectable pharmaceutical composition and a kit containing said pharmaceutical composition, wherein said pharmaceutical composition comprises: gabapentin and a pharmaceutically acceptable solvent.

II. Claims 46-50 are drawn to a process for preparing an injectable gabapentin composition.

Inventions I and II are related as a product and a method of making said product. The inventions can be shown to be distinct if either or both of the following can be shown that: (1) the method for making the product as claimed can be practiced with another materially different product; or (2) the product as claimed can be made by another method that is materially different from the instantly claimed method of making said product (MPEP § 806.05(f)). In the instant case, the pharmaceutical composition as claimed in Invention I can be made by another method that is materially different from the method claimed in Invention II. For example, as opposed to making said pharmaceutical composition comprising the steps of: (a) mixing gabapentin in a diluent to form a fluid composition; (b) determining the tonicity of said fluid composition; and if necessary, (c) adding a tonicity adjusting agent to said fluid composition to obtain a tonicity from about 290 mOsm to about 320 mOsm, said pharmaceutical composition may alternatively be made by a materially different method comprising the steps of: (a) combining a pharmaceutically active compound with a pharmaceutically acceptable excipient or vehicle, such as artificial cerebrospinal fluid, which already possesses a desired isotonicity suitable for direct intraspinal administration of said compound into the central nervous system, as described in Pre-Grant Patent Application Publication Number US2003/0055004, which was filed by Abood et al. ([0057]), thereby

avoiding the additional step(s) of having to determine tonicity and, if necessary, adding a tonicity adjusting agent to obtain a tonicity from about 290 mOsm to about 320 mOsm.

Because these inventions are distinct for the reasons given above and the search required for Group I is not required for Group II, restriction for examination purposes as indicated is proper.

Conclusion to Restriction Requirement

The Examiner has required restriction between product and methods of making claims. Where Applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn methods of making claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. Methods of making claims that depend from or otherwise include all the limitations of the patentable product will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. If claims are added after the election, Applicants must explicitly indicate which claims are readable upon the elected species. See MPEP § 809.02(a). Amendments submitted after final rejection are governed by 37 CFR 1.116. Amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined methods of making claims will be withdrawn, and the rejoined methods of making claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. §§ 101, 102, 103 and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and methods of making claims may be maintained. Withdrawn methods of making claims that are not commensurate in scope with an allowed product claim will not be rejoined.

See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai*, *In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the methods of making claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. Failure to do so may result in a loss of the right to rejoinder. Further, note that the prohibition against double patenting rejections of 35 U.S.C. § 121 does not apply where the restriction requirement is withdrawn by the Examiner before the patent issues. See MPEP § 804.01.

Applicants are reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR § 1.48(b) if one or more of the currently named Inventors is no longer an actual Inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR § 1.48(b) and by the fee required under 37 CFR § 1.17(i).

During a telephone conversation with Mr. Keith M. Campbell, Esq. on Tuesday, November 16, 2005, at approximately 4:30 P.M., a provisional election was made *without traverse* to prosecute the Invention of Group I, claims 1-45 and 51. As a result and pursuant to 37 CFR § 1.142(b), claims 46-50 are withdrawn from further consideration by the Examiner as being drawn to a non-elected invention.

Status of Claims

As previously discussed, claims 46-50 are withdrawn from further consideration as being drawn to a non-elected invention. On the other hand, claims 1-45 and 51 are drawn to the elected Invention of Group I. As a result, claims 1-45 and 51 are currently pending and therefore examined herein on the merits for patentability.

Provisional Nonstatutory Double Patenting

A nonstatutory double patenting rejection of the "obviousness-type" is based on a judicially created doctrine grounded in public policy so as to prevent not only the unjustified or improper timewise extension of the "right to exclude" granted by a patent, but also possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969); *In re White*, 405 F.2d 904, 160 USPQ 417 (CCPA 1969); *In re Schneller*, 397 F.2d 350, 158 USPQ 210 (CCPA 1968); and *In re Sarett*, 327 F.2d 1005, 140 USPQ 474 (CCPA 1964).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned or assigned with this application. See 37 CFR 1.130(b). Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

When considering whether the invention defined in a claim of an application is an obvious variation of the invention defined in the claim of a patent, the disclosure of the patent may not be used as prior art. See MPEP § 804. However, this does not mean that one is absolutely precluded from all use of the patent disclosure. See MPEP § 804. For example, the specification can always be used as a dictionary to learn the meaning of a term in the patent claim. *In re Boylan*, 392 F.2d 1017, 157 USPQ 370 (CCPA 1968). Furthermore, ***those portions of the specification which provide support for the patent claims may also be examined and considered*** when addressing the issue of whether a claim in the application defines an obvious variation of an invention claimed in the patent. *In re Vogel*, 422 F.2d 438,

441-442, 164 USPQ 619, 622 (CCPA 1970). The court in *Vogel* stated that one must first "determine how much of the patent disclosure pertains to the invention claimed in the patent" because only "[t]his portion of the specification supports the patent claims and may be considered." The court in *Vogel* also pointed out that "this use of the disclosure is not in contravention of the cases forbidding its use as prior art, nor is it applying the patent as a reference under 35 U.S.C. § 103, since only the disclosure of the invention claimed in the patent may be examined."

1. Claims 1-29, 34-44 and 51 of the instant application (10/808129) are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over conflicting claims 1-28 and 58-59 of copending U.S. Patent Application Serial Number 10/807827 (hereinafter the conflicting Hildebrand '827 application).

More specifically, claims 1-29, 34-44 and 51 of the instant application are directed to a heat sterilized injectable pharmaceutical composition comprising an aqueous saline solution of gabapentin in combination with an additional therapeutic agent selected from the following: sodium valproate, midazolam and baclofen; wherein said gabapentin is present in said aqueous saline solution at a concentration of greater than about 30 mg/mL; wherein said aqueous saline solution has a pH between about 4 and about 9; wherein said aqueous saline solution has a tonicity of about 250 mOsm, which is substantially isotonic with cerebrospinal fluid; wherein said aqueous saline solution is substantially free of preservatives and buffers; wherein said heat sterilized injectable pharmaceutical composition is packaged within a kit that further comprises instructions.

Claims 1-28 and 58-59 of the conflicting Hildebrand '827 application are directed to a system comprising an implantable pump, which is coupled to a reservoir and a catheter, for intrathecal

administration of an injectable pharmaceutical composition into cerebrospinal fluid, wherein said injectable pharmaceutical composition comprises an aqueous saline solution of gabapentin in combination with an additional therapeutic agent selected from the following: sodium valproate, midazolam and baclofen; wherein said gabapentin is present in said aqueous saline solution at a concentration of greater than about 30 mg/mL; wherein said aqueous saline solution has a pH between about 4 and about 9; wherein said aqueous saline solution has a tonicity that is substantially isotonic with cerebrospinal fluid; wherein said aqueous saline solution is substantially free of preservatives and buffers.

Although the aforementioned claims of the conflicting Hildebrand '827 application do not explicitly recite the instantly claimed tonicity of about 250 mOsm, it would have been prima facie obvious to one of ordinary skill in the art at the time the instant application was filed to modify the tonicity of said aqueous saline solution to about 250 mOsm, as the conflicting Hildebrand '827 application teaches intrathecal administration of said injectable pharmaceutical composition comprising said aqueous saline solution into cerebrospinal fluid ([0047]-[0048]). Therefore, one of ordinary skill in the art would have been motivated to modify the tonicity of said aqueous saline solution to about 250 mOsm so as to achieve an injectable pharmaceutical composition comprising said aqueous saline solution that is isotonic with, and thereby suitable for intrathecal administration into, cerebrospinal fluid. In addition, although the aforementioned claims of the conflicting Hildebrand '827 application do not explicitly recite heat sterilization of said injectable pharmaceutical composition, the conflicting Hildebrand '827 application teaches utilizing an autoclave or a filter as a means for sterilization ([0046]). The utilization of an autoclave, as opposed to a filter, does not render the injectable pharmaceutical composition of the conflicting Hildebrand '827 application patentably distinct from the heat sterilized injectable pharmaceutical composition of the instant application. "[E]ven though product-by-process

claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." See In re Thorpe, 227 USPQ 964, 966 (Fed. Cir. 1985). Furthermore, although the aforementioned claims of the conflicting Hildebrand '827 application do not explicitly recite a kit comprising said heat sterilized injectable pharmaceutical composition packaged with instructions, it would have been prima facie obvious to one of ordinary skill in the art at the time the instant application was filed to incorporate into a kit not only said system comprising said heat sterilized injectable pharmaceutical composition, but also instructions directed to and enabling for the corresponding use and the administration thereof by an end user, such as a patient, physician or nurse.

In conclusion, although claims 1-29, 34-44 and 51 of the instant application are not identical to claims 1-28 and 58-59 of the conflicting Hildebrand '827 application, the aforementioned claims are not patentably distinct each from the other because said claims are substantially overlapping in scope.

2. Claims 1-45 and 51 of the instant application (10/808129) are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over conflicting claims 1-27 and 51 of copending U.S. Patent Application Serial Number 10/807828 (hereinafter the conflicting Hildebrand '828 application).

More specifically, claims 1-45 and 51 of the instant application are directed to a heat sterilized injectable pharmaceutical composition comprising an aqueous saline solution of gabapentin in combination with an additional therapeutic agent selected from the following: baclofen, morphine and

hydromorphone; wherein said morphine may be present at a concentration from about 10 mg/mL to about 50 mg/mL; wherein said hydromorphone may be present at a concentration from about 1 mg/mL to about 20 mg/mL; wherein said gabapentin is present in said aqueous saline solution at a concentration of greater than about 30 mg/mL; wherein said aqueous saline solution has a pH between about 4 and about 9; wherein said aqueous saline solution has a tonicity of about 250 mOsm, which is substantially isotonic with cerebrospinal fluid; wherein said aqueous saline solution is substantially free of preservatives and buffers; wherein said heat sterilized injectable pharmaceutical composition is packaged within a kit that further comprises instructions.

Claims 1-27 and 51 of the conflicting Hildebrand '828 application are directed to a system comprising an implantable pump, which is coupled to a reservoir and a catheter, for intrathecal administration of an injectable pharmaceutical composition into cerebrospinal fluid, wherein said injectable pharmaceutical composition comprises an aqueous saline solution of gabapentin in combination with an additional therapeutic agent selected from the following: baclofen, morphine and hydromorphone; wherein said morphine may be present at a concentration from about 25 mg/mL to about 50 mg/mL ([0047]); wherein said hydromorphone may be present at a concentration from about 1.0 mg/mL to about 20 mg/mL ([0047]); wherein said gabapentin is present in said aqueous saline solution at a concentration of greater than about 30 mg/mL; wherein said aqueous saline solution has a pH between about 4 and about 9; wherein said aqueous saline solution has a tonicity that is substantially isotonic with cerebrospinal fluid; wherein said aqueous saline solution is substantially free of preservatives and buffers.

Although the aforementioned claims of the conflicting Hildebrand '828 application do not explicitly recite the instantly claimed tonicity of about 250 mOsm, it would have been prima facie obvious to one of ordinary skill in the art at the time the instant application was filed to modify the

tonicity of said aqueous saline solution to about 250 mOsm, as the conflicting Hildebrand '828 application teaches intrathecal administration of said injectable pharmaceutical composition comprising said aqueous saline solution into cerebrospinal fluid ([0043]-[0044]). Therefore, one of ordinary skill in the art would have been motivated to modify the tonicity of said aqueous saline solution to about 250 mOsm so as to achieve an injectable pharmaceutical composition comprising said aqueous saline solution that is isotonic with, and thereby suitable for intrathecal administration into, cerebrospinal fluid. In addition, although the aforementioned claims of the conflicting Hildebrand '828 application do not explicitly recite heat sterilization of said injectable pharmaceutical composition, the conflicting Hildebrand '828 application teaches utilizing an autoclave or a filter as a means for sterilization ([0041]). The utilization of an autoclave, as opposed to a filter, does not render the injectable pharmaceutical composition of the conflicting Hildebrand '828 application patentably distinct from the heat sterilized injectable pharmaceutical composition of the instant application. "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." See In re Thorpe, 227 USPQ 964, 966 (Fed. Cir. 1985). Furthermore, although the aforementioned claims of the conflicting Hildebrand '828 application do not explicitly recite a kit comprising said heat sterilized injectable pharmaceutical composition packaged with instructions, it would have been prima facie obvious to one of ordinary skill in the art at the time the instant application was filed to incorporate into a kit not only said system comprising said heat sterilized injectable pharmaceutical composition, but also instructions

directed to and enabling for the corresponding use and the administration thereof by an end user, such as a patient, physician or nurse.

In conclusion, although claims 1-45 and 51 of the instant application are not identical to claims 1-27 and 51 of the conflicting Hildebrand '828 application, the aforementioned claims are not patentably distinct each from the other because said claims are substantially overlapping in scope.

3. Claims 1-45 and 51 of the instant application (10/808129) are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over conflicting claims 1-48 of copending U.S. Patent Application Serial Number 10/808054 (hereinafter the conflicting Hildebrand '054 application).

More specifically, claims 1-45 and 51 of the instant application are directed to a heat sterilized injectable pharmaceutical composition comprising an aqueous saline solution of gabapentin in combination with an additional therapeutic agent selected from the following: sodium valproate, midazolam, baclofen, morphine and hydromorphone; wherein said morphine may be present at a concentration from about 10 mg/mL to about 50 mg/mL; wherein said hydromorphone may be present at a concentration from about 1 mg/mL to about 20 mg/mL; wherein said gabapentin is present in said aqueous saline solution at a concentration of greater than about 30 mg/mL; wherein said aqueous saline solution has a pH between about 4 and about 9; wherein said aqueous saline solution has a tonicity of about 250 mOsm, which is substantially isotonic with cerebrospinal fluid; wherein said aqueous saline solution is substantially free of preservatives and buffers; wherein said heat sterilized injectable pharmaceutical composition is packaged within a kit that further comprises instructions.

Claims 1-48 of the conflicting Hildebrand '054 application are directed to a system comprising an implantable pump, which is coupled to a reservoir and a catheter, for intrathecal administration of a heat sterilized injectable pharmaceutical composition into cerebrospinal fluid, wherein said heat sterilized injectable pharmaceutical composition comprises an aqueous saline solution of gabapentin in combination with an additional therapeutic agent selected from the following: sodium valproate, midazolam, baclofen, morphine and hydromorphone; wherein said morphine may be present at a concentration from about 10 mg/mL to about 50 mg/mL; wherein said hydromorphone may be present at a concentration from about 1 mg/mL to about 20 mg/mL; wherein said gabapentin is present in said aqueous saline solution at a concentration of greater than about 30 mg/mL; wherein said aqueous saline solution has a pH between about 4 and about 9; wherein said aqueous saline solution has a tonicity of about 250 mOsm, which is substantially isotonic with cerebrospinal fluid; wherein said aqueous saline solution is substantially free of preservatives and buffers.

Although the aforementioned claims of the conflicting Hildebrand '054 application do not explicitly recite a kit comprising said heat sterilized injectable pharmaceutical composition packaged with instructions, it would have been prima facie obvious to one of ordinary skill in the art at the time the instant application was filed to incorporate into a kit not only said system comprising said heat sterilized injectable pharmaceutical composition, but also instructions directed to and enabling for the corresponding use and the administration thereof by an end user, such as a patient, physician or nurse.

In conclusion, although claims 1-45 and 51 of the instant application are not identical to claims 1-48 of the conflicting Hildebrand '054 application, the aforementioned claims are not patentably distinct each from the other because said claims are substantially overlapping in scope.

4. Claims 1-26, 34-41 and 51 of the instant application (10/808129) are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over conflicting claims 1-38 of copending U.S. Patent Application Serial Number 10/8080113 (hereinafter the conflicting Hildebrand '054 application).

More specifically, claims 1-26, 34-41 and 51 of the instant application are directed to a heat sterilized injectable pharmaceutical composition comprising an aqueous saline solution of gabapentin; wherein said gabapentin is present in said aqueous saline solution at a concentration of greater than about 30 mg/mL; wherein said aqueous saline solution has a pH between about 4 and about 9; wherein said aqueous saline solution has a tonicity of about 250 mOsm, which is substantially isotonic with cerebrospinal fluid; wherein said aqueous saline solution is substantially free of preservatives and buffers; wherein said heat sterilized injectable pharmaceutical composition is packaged within a kit that further comprises instructions.

Claims 1-38 of the conflicting Hildebrand '113 application are directed to a method of making a heat sterilized injectable pharmaceutical composition comprising gabapentin and a pharmaceutically acceptable vehicle; wherein said gabapentin is present in said aqueous saline solution at a concentration of greater than about 30 mg/mL; wherein said aqueous saline solution is substantially free of preservatives and buffers.

Therefore, said heat sterilized injectable pharmaceutical composition or product claims of the instant invention are obvious over the claims of the conflicting Hildebrand '113 application, which are directed to a method of making said heat sterilized injectable pharmaceutical composition or product, because the method of making claims recite the product claimed therein. In addition, although the aforementioned claims of the conflicting Hildebrand '113 application do not explicitly recited the

instantly claimed aqueous saline solution as being the pharmaceutically acceptable vehicle, the conflicting Hildebrand '113 application teaches that said heat sterilized injectable pharmaceutical composition comprises an aqueous saline (sodium chloride) solution of gabapentin ([0020]-[0021] and [0027]-[0028]).

With respect to claims 23-24 and 34 of the instant application, although the aforementioned claims of the conflicting Hildebrand '113 application do not explicitly recite that the pharmaceutically acceptable vehicle has a pH between about 4 and about 9, the conflicting Hildebrand '113 application explicitly teaches that said heat sterilized injectable pharmaceutical composition comprises an aqueous saline solution of gabapentin, wherein said aqueous saline solution has a pH between about 4 and about 9 ([0020]-[0021], [0023] and [0027]-[0028]).

With respect to claims 1, 20-22 and 34 of the instant application, although the aforementioned claims of the conflicting Hildebrand '113 application do not explicitly recite the instantly claimed tonicity of about 250 mOsm, it would have been prima facie obvious to one of ordinary skill in the art at the time the instant application was filed to modify the tonicity of said pharmaceutically acceptable vehicle comprising said aqueous saline solution to about 250 mOsm, as the conflicting Hildebrand '113 application explicitly teaches intrathecal administration of said injectable pharmaceutical composition comprising said aqueous saline solution into cerebrospinal fluid ([0024]). Therefore, one of ordinary skill in the art at the time the instant application was filed would have been motivated to modify the tonicity of said aqueous saline solution to about 250 mOsm so as to achieve an injectable pharmaceutical composition comprising said aqueous saline solution that is isotonic with, and thereby suitable for intrathecal administration into, cerebrospinal fluid.

With respect to claims 35-37 of the instant application, although the aforementioned claims of the conflicting Hildebrand '113 application do not explicitly recite a kit comprising said heat sterilized

injectable pharmaceutical composition packaged with instructions, it would have been prima facie obvious to one of ordinary skill in the art at the time the instant application was filed to incorporate into a kit not only said system comprising said heat sterilized injectable pharmaceutical composition, but also instructions directed to and enabling for the corresponding use and the administration thereof by an end user, such as a patient, physician or nurse.

In conclusion, although the product claims 1-26, 34-41 and 51 of the instant application are not identical to the method of making claims 1-38 of the conflicting Hildebrand '113 application, the aforementioned claims are not patentably distinct each from the other because the method of making claims recite the product claimed therein.

Claim Rejections - 35 U.S.C. § 103

The following is a quotation of the appropriate paragraph of 35 U.S.C. § 103, which forms the basis of the obviousness rejections as set forth under this particular section of the Official Action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

1. Claims 1-45 and 51 are rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Pre-Grant Patent Application Publication Number 2001/0036943 (hereinafter the Coe '943 publication).

With respect to claims 1-45 and 51 of the instant application, the Coe '943 publication teaches a sterile injectable pharmaceutical composition ([0004], [0283], [0370] and [0372]), which may comprise: an anticonvulsant analgesic, such as gabapentin ([0006], [0138] and [0270]); an opioid analgesic, such as morphine and hydromorphone (a.k.a., Dilaudid) ([0004], [0006], [0138] and [0270]); and a

pharmaceutically acceptable carrier ([0004], [0006], [0368] and [0369]). Gabapentin may be present in an amount from 0.1% by weight to 95% by weight of said pharmaceutical composition ([0373]) and parenterally administered ([0283] and [0370]) in an amount from 10.0 mg/kg/day to 35.0 mg/kg/day ([0315]). Morphine may be present in an amount from 0.1% by weight to 95% by weight of said pharmaceutical composition ([0373]) and parenterally administered ([0283] and [0370]) in an amount from 0.1 mg/kg/day to 4.0 mg/kg/day ([0303]). Hydromorphone may be present in an amount from 0.1% by weight to 95% by weight of said pharmaceutical composition ([0373]) and parenterally administered ([0283] and [0370]) in an amount from 0.01 mg/kg/day to 2.0 mg/kg/day ([0301]). The pharmaceutically acceptable carrier is a sterile aqueous isotonic saline solution ([0370]). In regard to claims 25-26 and 34 in particular, the Coe '943 publication is utterly devoid of any teachings of the utilization of preservatives and merely mentions that said sterile aqueous isotonic saline solution may be suitably buffered, *if necessary*, so as to render said injectable pharmaceutical composition possessing an osmolality suitable for parenteral administration.

With respect to claims 1 and 38 of the instant application, the Coe '943 publication does not explicitly teach either a specific numerical value of osmolality that is isotonic with cerebrospinal fluid as recited in claim 1 of the instant application, or a sterile injectable pharmaceutical composition that comprises less than 0.9% weight per volume of sodium chloride as recited in claim 38 of the instant application. However, the Coe '943 publication does teach that said sterile injectable pharmaceutical composition comprises a sterile aqueous isotonic saline solution for parenteral administration ([0283], [0368], [0370] and [0372]). Parenteral administration by definition includes any route of administration (i.e., intrathecal or epidural) other than enteral (i.e., oral) administration. Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the instant application was filed to utilize

an appropriate weight per volume of sodium chloride so as to render an sterile injectable pharmaceutical composition comprising a sterile aqueous isotonic saline solution possessing a desired osmolality that is isotonic with cerebrospinal fluid thereby rendering said sterile injectable pharmaceutical composition suitable for parenteral administration via intrathecal or epidural injection.

With respect to claims 27-33 and 42-45 of the instant application, although the Coe '943 publication teaches that said sterile injectable pharmaceutical composition *may* comprise an anticonvulsant analgesic in combination with an opioid analgesic for the treatment of pain ([0006], [0138], [0270], [0368] and [0373]), the Coe '943 publication does not explicitly teach the instantly claimed composition comprising gabapentin in combination with morphine and/or hydromorphone. However, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the instant application was filed to in fact utilize gabapentin in combination with morphine and/or hydromorphone, as the Coe '943 publication teaches that not only gabapentin, but also morphine and hydromorphone are particularly useful in the treatment of pain. Therefore, one of ordinary skill in the art would have been motivated at the time the instant application was filed to combine an anticonvulsant analgesic, such as gabapentin, together with an opioid analgesic, such as morphine and/or hydromorphone, within said sterile injectable pharmaceutical composition so as to impart desired analgesic properties to said sterile injectable pharmaceutical composition, thereby rendering said sterile injectable pharmaceutical composition particularly useful in the treatment pain, as suggested by the Coe '943 publication. In addition, the Coe '943 publication also teaches that: said gabapentin may be present in an amount from 0.1% by weight to 95% by weight of said pharmaceutical composition ([0373]) and parenterally administered ([0283] and [0370]) in an amount from 10.0 mg/kg/day to 35.0 mg/kg/day ([0315]); said morphine may be present in an amount from 0.1% by weight to 95% by weight of said pharmaceutical

composition ([0373]) and parenterally administered ([0283] and [0370]) in an amount from 0.1 mg/kg/day to 4.0 mg/kg/day ([0303]); and said hydromorphone may be present in an amount from 0.1% by weight to 95% by weight of said pharmaceutical composition ([0373]) and parenterally administered ([0283] and [0370]) in an amount from 0.01 mg/kg/day to 2.0 mg/kg/day ([0301]). It is well within the purview of the skilled artesian to determine the desired optimal workable concentrations of gabapentin, morphine and hydromorphone by systematically adjusting the injectable dosage amounts of gabapentin, morphine and hydromorphone in a given per unit volume of diluent during the course of routine experimentation. "Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." See *In re Aller*, 105 USPQ 233, 235 (CCPA 1955). "The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages." See *Peterson*, 65 USPQ2d 1379, 1382 (Fed. Cir. 2003).

With respect to claims 23-24 and 34 of the instant application, although the Coe '943 publication does not explicitly teach a specific pH that is physiologically similar to that of cerebrospinal fluid, the Coe '943 publication does teach that said sterile injectable pharmaceutical composition comprises a sterile aqueous isotonic saline solution, which is suitably buffered, if necessary, for parenteral administration and is readily obtainable by standard techniques well known to those of ordinary skill in the art ([0283], [0368], [0370] and [0372]). Parenteral administration by definition includes any route of administration (i.e., intrathecal or epidural) other than enteral (i.e., oral) administration. Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the instant application was filed to utilize a pH buffer, if necessary, so as to render an injectable pharmaceutical composition comprising a sterile aqueous isotonic saline solution possessing a desired pH suitable for parenteral administration so as to

render an sterile injectable pharmaceutical composition comprising a sterile aqueous isotonic saline solution possessing a desired pH that is physiologically similar to that of cerebrospinal fluid thereby rendering said sterile injectable pharmaceutical composition suitable for parenteral administration via intrathecal or epidural injection.

With respect to claims 35-37 of the instant application, although the Coe '943 publication does not explicitly teach a kit comprising said injectable pharmaceutical composition packaged with instructions, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the instant application was filed to incorporate into a kit not only said system comprising said injectable pharmaceutical composition, but also instructions directed to and enabling for the corresponding use and the administration thereof by an end user, such as a patient, physician or nurse.

With respect to claim 51 of the instant application, although the Coe 943 publication does not explicitly teach that said sterile injectable pharmaceutical composition is heat sterilized, the Coe '943 publication explicitly teaches that said sterile injectable pharmaceutical composition is prepared by methods readily known to those of ordinary skill in the art (1975) ([0004], [0283], [0370] and [0372]). Therefore, it would have been obvious to one of ordinary skill in the art at the time the instant application was filed to utilize an autoclave or a filter as a means of sterilizing said sterile injectable pharmaceutical composition. One of ordinary skill in the art would have been motivated to heat said injectable pharmaceutical composition to a temperature sufficient to thereby sterilize and increase the shelf life of said injectable pharmaceutical composition. In addition, utilization of a filter, as opposed to an autoclave, does not render the injectable pharmaceutical composition of the Coe '943 publication patentably distinct from the heat sterilized injectable pharmaceutical composition of the instant application. "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is

based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." See *In re Thorpe*, 227 USPQ 964, 966 (Fed. Cir. 1985).

2. Claims 35-36 are rejected under 35 U.S.C. § 103(a) as being unpatentable over the Coe '943 publication in view of U.S. Pre-Grant Patent Application Publication Number 2003/0119756 (hereinafter the Gaeta '756 publication).

With respect to claims 35-36 of the instant application, although the Coe '943 publication teaches an injectable pharmaceutical composition ([0004], [0283] and [0370]) that may comprise an anticonvulsant, such as gabapentin ([0006], [0138] and [0270]), wherein said gabapentin may be administered parenterally ([0283] and [0370]), the Coe '943 publication does not explicitly teach a kit comprising said injectable pharmaceutical composition packaged with instructions indicating that said injectable pharmaceutical composition may be administered intrathecally. However, the Gaeta '756 publication teaches a kit ([0017] and [0049]) comprising: an injectable pharmaceutical composition comprising an anticonvulsant, such as gabapentin, which may be parenterally administered intrathecally into the cerebral spinal fluid ([0017], [0032], [0033] and [0044]); and instructions describing how to use said injectable pharmaceutical composition ([0049]). Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the instant application was filed to incorporate the injectable pharmaceutical composition, which may comprise an anticonvulsant such as gabapentin, for parenteral administration, as taught by the Coe '943 publication, into a kit also comprising instructions describing how to use said injectable pharmaceutical composition. One of ordinary skill in the art would have been

motivated to incorporate said injectable pharmaceutical composition comprising gabapentin into a kit, which also comprises instructions describing how to intrathecally administer said injectable pharmaceutical composition into the cerebral spinal fluid, as suggested by Gaeta '756 publication.

3. Claims 35 and 37 are rejected under 35 U.S.C. § 103(a) as being unpatentable over the Coe '943 publication in view of U.S. Patent 6,495,601 (hereinafter the Hochman '601 patent)

With respect to claims 35 and 37 of the instant application, although the Coe '943 publication teaches an injectable pharmaceutical composition ([0004], [0283] and [0370]) that may comprise an anticonvulsant, such as gabapentin ([0006], [0138] and [0270]), wherein said gabapentin may be administered parenterally ([0283] and [0370]), the Coe '943 publication does not explicitly teach a kit comprising said injectable pharmaceutical composition packaged with instructions indicating that said injectable pharmaceutical composition be placed into a system comprising an implantable pump, which is coupled to a reservoir and a catheter. However, the Hochman '601 patent teaches a kit (column 15, lines 51-62) comprising: an injectable pharmaceutical composition, which may comprise an anticonvulsant and antiepileptic, such as gabapentin (column 14, lines 42-67; and column 15, lines 1-47), which may be parenterally administered by intracranial or epidural administration into the cerebrospinal fluid (column 12, lines 60-67; and column 14, lines 9-12) via a system comprising an implantable pump (column 13, lines 23-33 and 38-39). Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the instant application was filed to incorporate the injectable pharmaceutical composition, which may comprise an anticonvulsant such as gabapentin, for parenteral administration, as taught by the Coe '943 publication, into a kit also comprising a system equipped with an implantable pump for intracranial or epidural administration of said injectable pharmaceutical composition into the

cerebrospinal fluid. One of ordinary skill in the art would have been motivated to incorporate said injectable pharmaceutical composition comprising gabapentin into a kit also comprising a system equipped with an implantable pump for intracranial or epidural administration of said injectable pharmaceutical composition into the cerebrospinal fluid, as suggested by the Hochman '601 patent. In addition, it would have been prima facie obvious to one of ordinary skill in the art at the time the instant application was filed to incorporate into a kit not only said system comprising said injectable pharmaceutical composition, but also instructions directed to and enabling for the corresponding use and the administration thereof by an end user, such as a patient, physician or nurse. Furthermore, it would have been obvious to one of ordinary skill in the art at the time the instant application was filed to couple a reservoir and a catheter to the implantable pump of the system taught in the Hochman '601 patent to provide for the storage and subsequent delivery of said injectable pharmaceutical composition into the cerebrospinal fluid.

Therefore, the claimed invention, as a whole, would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, because each and every element of the claimed invention, as a whole, would have been reasonably suggested by the teachings of the cited prior art references.

Conclusion

Claims 46-50 were withdrawn from consideration as being drawn to a non-elected invention. Claims 1-45 and 51 are rejected.

Relevant Prior Art

The following is a list of prior art patents and pre-grant patent application publications made of record and considered to be pertinent to the Applicants' disclosure, but are not however currently relied upon in construing the claim rejections as set forth herein:

U.S. Pre-Grant Patent Application Publication Number 2002/0107265 ([0056], [0059], [0061], [0063], [0067], [0085]-[0087], [0093]; and
U.S. Patent Number 4,755,388 (column 3, lines 10-20; and column 5, lines 6-9).

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David P. Stitzel, Esq. whose telephone number is 571-272-8508. The examiner can normally be reached on Monday-Friday, from 7:30AM-6:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached at 571-272-0629. The central fax number for the USPTO is 571-273-8300.

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